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PATENT
Docket No. 30414/2000321
Client Ref. 11D10

Exhibit A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Chatterjee et al.

Serial No.: 08/766,350

Filing Date: December 13, 1996

For: MURINE ANTI-IDIOTYPE ANTIBODY
11D10 AND METHODS OF USE
THEREOF

Examiner: Stephen Rawlings

Group Art Unit: 1642

**DECLARATION OF MALAYA BHATTACHARYA-CHATTERJEE
PURSUANT TO 37 C.F.R § 1.132**

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Malaya Bhattacharya-Chatterjee, Ph.D., declare as follows:

1. I am an inventor of the above-referenced patent application, under the name of Malaya Chatterjee.
2. I am a Professor of Internal Medicine at the University of Cincinnati. I am currently also an adjunct Professor in the Department of Internal Medicine at the University of Kentucky. My research expertise includes the fields of immunochemistry and molecular oncology.

3. In collaboration with the other inventors of the above-referenced patent application, I developed and cloned the 11D10 antibody-producing hybridoma cell line.

Lack of availability of anti-idiotypic antibody 11D10 and the hybridoma cell line producing 11D10

4. The 11D10-producing cells, the re-cloned 11D10 cell line, the predecessors and progeny thereof, and the antibody produced thereby has been maintained exclusively under the control of myself and the other inventors of the above-referenced patent application. There has been no free exchange of 11D10 or the cell line producing 11D10. Neither 11D10 nor the cell line producing 11D10 was released to the public before the filing of the above-referenced patent application (or previously-filed provisional application 60/031,306, filed December 20, 1995), and both remain under strict supervision and control.

5. The DNA and amino acid sequences of the 11D10 variable region genes were determined by co-inventor Dr. Sunil Chatterjee. The 11D10 sequence data was not disclosed before filing of the above-referenced application (or previously-filed provisional application 60/031,306, filed December 20, 1995) except under terms of confidentiality. The data were included in a grant application under terms of confidentiality, and it is my understanding that the data remained confidential until after filing the above-referenced application.

6. I understand that the Patent Office may question whether the public could have obtained the cell line or the antibody from the co-authors (or their laboratories) of certain publications. In particular, the following papers addressing 11D10 have been brought to my attention: (a) Bhattacharya-Chatterjee et al., "Anti-idiotypic antibodies as potential therapeutic agents for human breast cancer", in *Antigen and Antibody Molecular Engineering* (Ceriani, ed.) (1994), pages 139-148; (b) Bhattacharya Chatterjee et al., *Cancer Immunol. Immunother.* (1994) 38:75-82; (c) Chakraborty et al., *Proc. Am. Assoc. Cancer Res.* (1994), Abstract 2963; (d) Mukerjee et al. *Fed. Amer. Soc. Exp. Bio.* (1992) Abstract 6505; (e) Mukerjee et al., *Fed. Amer. Soc. Exp. Biol.* (1991) Abstract 7792; (f) Chakraborty et al., *Cancer Res.* (1995) 55:1525-1530.

7. The affiliation and role of the co-authors on these papers was as follows:

- I was lead scientist with a primary academic appointment in the Department of Gynecologic Oncology at Roswell Park Cancer Institute, Buffalo. (I later changed

my affiliation to the Markey Cancer Center at the University of Kentucky.) I was in charge of the laboratory where the 11D10 antibody was produced and tested, and maintained strict and exclusive control over the distribution of the 11D10 antibody and the antibody producing cell line. I distributed the antibody and cell line within the laboratory only on an as-needed basis to carry out experimental studies under my supervision. The cell line was not sent outside my laboratory, except with the understanding that it would not be distributed further and would continue to be maintained under strict and exclusive control of the named inventors of this patent application.

- *Ewe Mrozek, M.D.*, was a post-doctoral fellow working under my supervision in my laboratory at the time the experiments described in the paper (paper (a), above) were carried out. She participated in generation of the hybridoma cell line that produced 11D10, and worked under my direct supervision. When she left my laboratory, there was no reason for her to take 11D10 or the cell line producing 11D10 with her, nor did she have permission to do so. To the best of my knowledge and belief, she did not distribute the 11D10 antibody or the 11D10 antibody producing cell line outside the laboratory during the entire period she spent under my supervision, nor has she had possession of the 11D10 antibody or 11D10 producing cell line since leaving my laboratory.
- *Sonjoy Mukerjee* was a post-doctoral fellow working under my supervision in my laboratory at the time the experiments described in the papers (paper (a), (d), (e), and (f), above) were carried out. Under my direction, Dr. Mukerjee participated in generating and characterizing 11D10 antibody (such as performing Western blots). When he left my laboratory, there was no reason for him to take 11D10 antibody or the 11D10 antibody producing cell line with him, nor did he have permission to do so. To the best of my knowledge and belief, he did not distribute the 11D10 antibody or the 11D10 producing cell line outside the laboratory during the entire period he spent under my supervision, nor has he had possession of the 11D10 antibody or 11D10 producing cell line since leaving my laboratory.
- *Mala Chakraborty* was a post-doctoral fellow under my supervision in my laboratory at the time the experiments described in the papers (papers (c) and (f), above) were

carried out. Under my direction, Dr. Chakaborty participated in characterizing 11D10 antibody and assisted in carrying out the monkey studies using 11D10. When she left my laboratory, there was no reason for her to take 11D10 antibody or the 11D10 producing cell line with her, nor did she have permission to do so. To the best of my knowledge and belief, she did not distribute the 11D10 antibody or the 11D10 producing cell line outside the laboratory during the entire period she spent under my supervision, nor has she had possession of the 11D10 antibody or 11D10 producing cell line since leaving my laboratory.

- *Roberto Ceriani* is a research scientist who provided Ab1, the starting material which provided a basis for obtaining 11D10 (i.e., Ab1 was used for the immunization protocol which led to the generation of 11D10). Aside from providing Ab1, Dr. Ceriani did not participate in any way with the generation or characterization of 11D10. To the best of my knowledge and belief, he has never had possession of 11D10 antibody or the 11D10 producing cell line.
- *Heinz Köhler*, a research scientist and colleague, did not participate in any way with the generation or characterization of 11D10. To the best of my knowledge and belief, he has never had possession of 11D10 antibody or the 11D10 producing cell line.
- *M. Sherratt, M.D.*, was a researcher in my laboratory under my supervision when the monkey experiments described in reference (c) were being conducted. She performed T cell assays. When she left my laboratory, there was no reason for her to take the 11D10 antibody or the 11D10 producing cell line with her, nor did she have permission to do so. To the best of my knowledge and belief, she did not distribute the 11D10 antibody or the 11D10 antibody producing cell line outside the laboratory during the entire period she spent under my supervision, nor has she had possession of the 11D10 antibody or 11D10 producing cell line since leaving my laboratory.

8. Throughout the entire period between the time when the 11D10 antibody-producing cell line was obtained in my laboratory and the time when this patent application was filed in the U.S. Patent Office (as well as previously-filed provisional application 60/031,306, filed December 20, 1995), both the cell line and the antibody were maintained under the strict and exclusive control of myself and the other named inventors on the application. To the best of

my knowledge and belief, the public did not have access to the cell line or the antibody (other than patients in the clinical studies who received 11D10 antibody by injection under Dr. Kenneth Foon's direction and supervision) at any time before the filing of this patent application. I did not make the antibody or cell line available to the public, and I did not believe I was under any obligation to make the antibody or cell line available.

Inventorship

9. I understand that the Patent Office may question whether co-authors of the publications referenced in ¶ 6 of this declaration should also be named as inventor(s) on this application. More particularly, I understand that the Patent Office has requested information regarding the role of the co-authors with respect to generation of 11D10 antibody (including the 11D10 producing cell line).

I chose the protocols and criteria to be followed for developing and selecting the 11D10 antibody. I instructed Drs. Mrozek and Mukerjee to follow these protocols, and they reported the results of their experiments to me. I chose 11D10 as the most desirable antibody.

As summarized below, none of the co-authors made independent contributions to generation of 11D10 antibody or the 11D10 producing cell line (i.e., they were working under my direct supervision). In some cases, co-authors did not make any contribution to generation of 11D10 antibody or the 11D10 producing cell line.

- *Dr. Ceriani's* role was confined to merely providing my laboratory with the Ab1 used, BrE-1. Dr. Ceriani did not perform any work or make any contributions with respect to developing or characterizing 11D10 or the 11D10 producing cell line, other than providing a starting material.
- *Dr. Kohler* did not participate in generating or characterizing 11D10 antibody or the 11D10 producing cell line.
- *Dr. Mrozek* participated in generating the 11D10 producing cell line, but only under my direct supervision. She did not make any independent contributions to generating 11D10 or the 11D10 producing cell line.
- *Dr. Mukerjee* participated in generating and characterizing 11D10 antibody (such as Western blots), but only under by direct supervision. He did not make any independent contributions to generating 11D10 or the 11D10 producing cell line.

- *Dr. Chakraborty* participated in characterizing 11D10 antibody and assisted in carrying out the monkey studies using 11D10, but only under my direct supervision. She did not make any independent contributions to generating 11D10 or the 11D10 producing cell line.
- *Dr. Sherrat* did not participate in generating or characterizing 11D10 or 11D10 producing cell line. She performed T cell assays in the monkey studies, which were performed after 11D10 had been generated. She did not make any contributions to generating 11D10 or the 11D10 producing cell line.

Deposit of the 11D10-producing cell line with the ATCC

10. The 11D10-producing cell line was deposited with the American Type Culture Collection on January 17, 1996, and given Accession Number HB12020.

11. The 11D10-producing cell line deposited with the ATCC is the same cell line that is described and claimed in the patent application and in previously-filed provisional application 60/031,306 (formerly 08/575,762), filed December 20, 1995.

12. The above culture has been deposited under conditions which assure that access to the culture will be irrevocably available during pendency of the patent application to one determined by the Assistant Commissioner to be entitled such access under 37 C.F.R. § 1.14 and 35 U.S.C. § 122 and, upon issuance of any patent on the above-identified application, to the general public without restriction; and that the deposited culture shall be stored with the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited culture and in any case, for a period of at least 30 years after the date of deposit or for the enforceable life of the patent, whichever period is longer.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

July 28, 2003
Date

Malaya Bhattacharya - Chatterjee
Malaya Bhattacharya-Chatterjee, Ph.D.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Chatterjee et al.

Serial No.: 08/766,350

Filing Date: December 13, 1996

For: MURINE ANTI-IDIOTYPE ANTIBODY
11D10 AND METHODS OF USE
THEREOF

Examiner: Stephen Rawlings

Group Art Unit: 1642

DECLARATION OF SUNIL K. CHATTERJEE PURSUANT TO 37 C.F.R. §1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Sunil K. Chatterjee, Ph.D., do hereby declare:

1. I am a co-inventor of the above-referenced patent application.

2. I am a Professor in the Department of Internal Medicine, University of Cincinnati.

My research expertise includes the field of molecular biology and genetic engineering.

3. I have obtained the nucleic acid sequence and the corresponding amino acid sequence for the light and heavy chain variable regions of antibody 11D10. This data, along with the method used to obtain it, described in the specification in Example 2 and Figures 1 and 2.

4. The heavy and light chain amino acid sequences were compared using the BLAST algorithm at the National Center for Biotechnology Information with all sequences available from the PDB, SwissProt, PIR, SPUpdate, GenPept, and GPUTupdate databases. The comparison was performed on January 19, 1996.

5. The 15 sequences matching most closely to the 11D10 heavy and light chain variable region sequences are shown in the patent application on page 117.

The comparison reveals the following:

- The 11D10 *light chain* variable region differs from the most closely matched previously known antibody sequences by at least 8 and more typically 10 or more substitution differences.
- No antibody was found using the same *heavy chain* V-D-J gene combination, indicating that the V-D-J splice employed in 11D10 is unusual.
- Antibodies apparently using the same *heavy chain* V gene element as 11D10 differed from 11D10 within this region by at least 13 substitutions and more typically by at least 16 substitution differences.

6. Figure 26(C) of the patent application provides a consensus analysis of the most closely matched sequences. The consensus sequence represents a prototype of the rearranged VJ light chain and VDJ heavy chain germ line sequences that were subsequently mutated to give the mature sequence found in 11D10. Identical residues are marked with a period and CDRs are overscored with asterisks. The 11D10 amino acid sequences differ in 7 positions from the prototype light chain variable region, and at least 11 positions from the heavy chain variable region. Accordingly, it is likely that at least about 18 mutation events occurred in the generation of 11D10, of which 9 are outside the CDRs.

7. The 11D10 producing cell line used in my laboratory was under my strict and exclusive control. These materials were provided to me for sequencing purposes. To the best of my knowledge and belief, no one in my laboratory took the 11D10 antibody or the 11D10 antibody producing cell line, nor did anyone have permission to do so.

8. Throughout the entire period from the time the 11D10 producing cell line was obtained by my laboratory and the time when this patent application was filed in the U.S. Patent Office (as well as the previously filed application 60/031,306, filed December 20, 1995), both the cell line and the antibody were maintained under the strict and exclusive control of myself and the other named inventors on the application. To the best of my knowledge and belief, the public did not have access to the cell line or the antibody (other than patients in the clinical studies who received 11D10 antibody by injection under Dr. Kenneth Foon's direction and supervision) at any time before the filing date of this patent application. I did not make the antibody or cell line available to the public, and I did not believe I was under any obligation to make the antibody or cell line available.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

July 25, 2003

Date

Sunil Chatterjee

Sunil K. Chatterjee, Ph.D.



PATENT
Docket No. 30414/2000322
Client Ref. 11D10

Exhibit B

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Malaya CHATTERJEE et al.

Serial No.: 08/836,455

Filing Date: May 9, 1997

For: MURINE MONOCLONAL ANTI-
IDIOTYPE 11D10 AND METHODS OF
USING THEREOF

Examiner: Stephen Rawlings

Group Art Unit: 1642

**DECLARATION OF MALAYA BHATTACHARYA-CHATTERJEE
PURSUANT TO 37 C.F.R § 1.132**

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Malaya Bhattacharya-Chatterjee, Ph.D., declare as follows:

1. I am an inventor named in the above-referenced patent application, under the name of Malaya Chatterjee.

2. I am a Professor of Internal Medicine at the University of Cincinnati. I am currently also an adjunct Professor in the Department of Internal Medicine at the University of Kentucky. My research expertise includes the fields of immunochemistry and molecular oncology.

3. In collaboration with the other inventors of the above-referenced patent application, I developed and cloned the 11D10 antibody-producing hybridoma cell line.

4. I understand that Chakraborty, et al., *Journal of Immunotherapy* (1995) 18(2):95-103 has been cited as the basis of a rejection of the claims of the above-referenced patent application under 35 U.S.C. § 102(a).

5. Chakraborty, et al., *Journal of Immunotherapy* (1995) 18(2):95-103, is an article describing my own work and the work of the other co-inventors of this application. As summarized below, none of the co-authors who are not co-inventors of this application made independent contributions to generation of 11D10 antibody or the 11D10 producing cell line.

6. The affiliation and role of the non-inventor co-authors on this paper with respect to generation of 11D10 antibody (including the 11D10 producing cell line) was as follows:

- *Mala Chakraborty* was a post-doctoral fellow under my supervision in my laboratory at the time the experiments described in the paper above was carried out. Under my direction, Dr. Chakraborty participated in characterizing 11D10 antibody and assisted in carrying out the monkey studies using 11D10, but only under my direct supervision. She did not make any independent contributions to generating 11D10 or the 11D10 producing cell line.
- *Heinz Köhler*, a research scientist and colleague, did not participate in any way with the generation or characterization of 11D10. To the best of my knowledge and belief, he has never had possession of 11D10 antibody or the 11D10 producing cell line.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

9-13-02
Date

Malaya Bhattacharya-Chatterjee
Malaya Bhattacharya-Chatterjee, Ph.D.

RECEIVED

SEP 08 1998

MORRISON & ECKERT

Office Action Summary



Application No.

08/836,455

Applicant(s)

Chatterjee et al

Examiner

Julie E. Reeves, Ph.D.

Group Art Unit

1642

- ☐ Responsive to communication(s) filed on _____.
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire zero month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 1-58 is/are pending in the application.
- Of the above, claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☐ Claim(s) _____ is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☒ Claims 1-58 are subject to restriction or election requirement.

Application Papers

- ☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☐ Notice of References Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Interview Summary, PTO-413
- ☒ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

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— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Art Unit: 1642

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-5, 20-37, 39-40, 42-43, 46-48, 54-56, drawn to monoclonal antibody 11D10, hybridoma expressing the antibody, polypeptides and vaccines comprising the 11D10 antigen binding region and the first method of use of eliciting an immune response by administering an effective amount of vaccine.

Group II, claim(s) 6-19, 38, 41, 44-45, 57-58, drawn to polynucleic acids that encode a polypeptide comprising the antigen binding region of monoclonal antibody 11D10.

Group III, claim(s) 49, drawn to a method for removing labeled anti-human milk fat globule antibody from an individual.

Group IV, claim(s) 50, drawn to a method for detecting the presence of an anti-human milk fat globule antibody.

Group V, claim(s) 51, drawn to a method for detecting an anti-human milk fat globule immunologic response.

Group VI, claim(s) 52, drawn to a method for detecting an antibody that binds to monoclonal antibody 11D10.

Art Unit: 1642

Group VII, claim(s) 53, drawn to a method of palliating human milk fat globule associated disease in an individual.

2. The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the protein and polynucleic acids of Groups I and II have different chemical properties which result in different biochemical, physiological and immunological properties. The methods of Groups I and Groups III-VIII involve different objectives, different endpoints, different protocols and materially different reagents. The examination of all groups would require different searches in the U.S. PATENT shoes and the scientific literature and would require the consideration of different patentability issues.

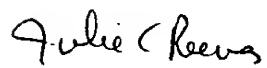
3. A telephone call was made to Catherine Polizzi on 3 Sept 1993 to request an oral election to the above restriction requirement, but did not result in an election being made.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Art Unit: 1642

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie E. Reeves, Ph.D. whose telephone number is (703) 308-7553.

A handwritten signature in cursive script that reads "Julie E. Reeves".

Julie E. Reeves, Ph.D.

September 3, 1998